



## Clinical trial results:

### **A Multicenter, Randomized, Double-Blind, Placebo-Controlled Phase 2 Study of Tabalumab in Combination with Bortezomib and Dexamethasone in Patients with Previously Treated Multiple Myeloma** **Summary**

EudraCT number	2011-005103-32
Trial protocol	GB ES GR PL DE NL IT
Global end of trial date	29 July 2014

#### **Results information**

Result version number	v1 (current)
This version publication date	09 April 2018
First version publication date	09 April 2018

#### **Trial information**

##### **Trial identification**

Sponsor protocol code	H9S-MC-JDCG
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##### **Additional study identifiers**

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01602224
WHO universal trial number (UTN)	-
Other trial identifiers	Trial Number: 14199

Notes:

##### **Sponsors**

Sponsor organisation name	Eli Lilly and Company
Sponsor organisation address	Lilly Corporate Center , Indianapolis, IN, United States, 46285
Public contact	Available Mon-Fri 9 AM - 5 PM EST, Eli Lilly and Company, 1 877-CTLilly,
Scientific contact	Available Mon-Fri 9 AM - 5 PM EST, Eli Lilly and Company, 1 877-285-4559,

Notes:

##### **Paediatric regulatory details**

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

## Results analysis stage

Analysis stage	Final
Date of interim/final analysis	29 July 2014
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	29 July 2014
Was the trial ended prematurely?	No

Notes:

## General information about the trial

Main objective of the trial:

The purpose of this study is to evaluate an investigational drug called tabalumab in participants with Multiple Myeloma (MM) who have tried at least one other therapy in the past. Tabalumab will be given in combination with standard doses of two other drugs that are often used to treat MM. Study doctors will collect information about the effectiveness and side effects of this therapy.

Protection of trial subjects:

This study was conducted in accordance with International Conference on Harmonization (ICH) Good Clinical Practice, and the principles of the Declaration of Helsinki, in addition to following the laws and regulations of the country or countries in which a study is conducted.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	12 June 2012
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

## Population of trial subjects

### Subjects enrolled per country

Country: Number of subjects enrolled	Brazil: 11
Country: Number of subjects enrolled	Canada: 4
Country: Number of subjects enrolled	France: 12
Country: Number of subjects enrolled	Germany: 4
Country: Number of subjects enrolled	Greece: 22
Country: Number of subjects enrolled	Italy: 12
Country: Number of subjects enrolled	Korea, Democratic People's Republic of: 23
Country: Number of subjects enrolled	Mexico: 6
Country: Number of subjects enrolled	Netherlands: 1
Country: Number of subjects enrolled	Poland: 24
Country: Number of subjects enrolled	Spain: 21
Country: Number of subjects enrolled	Taiwan: 18
Country: Number of subjects enrolled	Turkey: 17
Country: Number of subjects enrolled	United States: 29
Country: Number of subjects enrolled	United Kingdom: 16
Worldwide total number of subjects	220
EEA total number of subjects	112

Notes:

<b>Subjects enrolled per age group</b>	
In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	99
From 65 to 84 years	119
85 years and over	2

## Subject disposition

### Recruitment

Recruitment details: -

### Pre-assignment

Screening details:

Completers are defined as participants who died or had disease progression or completed treatment or did not complete treatment and were followed for survival data.

### Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Carer

### Arms

Are arms mutually exclusive?	Yes
<b>Arm title</b>	100 mg Tabalumab+Dexamethasone+Bortezomib

Arm description:

Tabalumab 100 milligram (mg) administered once intravenously (IV) over 30 minutes on Day 1 every 21 days for 8 cycles.

Dexamethasone 20 mg administered once orally on Days 1, 2, 4, 5, 8, 9, 11 and 12 every 21 days for 8 cycles.

Bortezomib 1.3 milligram per square meter (mg/m<sup>2</sup>) administered once subcutaneously (SQ) on Days 1, 4, 8 and 11 every 21 days for 8 cycles.

Arm type	Experimental
Investigational medicinal product name	Dexamethasone
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Dexamethasone 20 mg administered once orally on Days 1, 2, 4, 5, 8, 9, 11 and 12 every 21 days for 8 cycles.

Investigational medicinal product name	Bortezomib
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Bortezomib 1.3 mg/m<sup>2</sup> administered once SQ on Days 1, 4, 8 and 11 every 21 days for 8 cycles.

Investigational medicinal product name	100 mg Tabalumab
Investigational medicinal product code	
Other name	LY2127399
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Tabalumab 100 mg administered once IV over 30 minutes on Day 1 every 21 days for 8 cycles.

Dexamethasone 20 mg administered orally on Days 1, 2, 4, 5, 8, 9, 11 and 12 every 21 days for 8 cycles.

<b>Arm title</b>	300 mg Tabalumab+Dexamethasone+Bortezomib
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Arm description:

Tabalumab 300 mg administered once IV over 30 minutes on Day 1 every 21 days for 8 cycles.

Dexamethasone 20 mg administered orally on Days 1, 2, 4, 5, 8, 9, 11 and 12 every 21 days for 8 cycles.

Bortezomib 1.3 mg/m<sup>2</sup> administered once SQ on Days 1, 4, 8 and 11 every 21 days for 8 cycles.

Arm type	Experimental
Investigational medicinal product name	Dexamethasone
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Dexamethasone 20 mg administered once orally on Days 1, 2, 4, 5, 8, 9, 11 and 12 every 21 days for 8 cycles.

Investigational medicinal product name	Bortezomib
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Bortezomib 1.3 mg/m<sup>2</sup> administered once SQ on Days 1, 4, 8 and 11 every 21 days for 8 cycles.

Investigational medicinal product name	300 mg Tabalumab
Investigational medicinal product code	
Other name	LY2127399
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Tabalumab 300 mg administered once IV over 30 minutes on Day 1 every 21 days for 8 cycles.

Dexamethasone 20 mg administered orally on Days 1, 2, 4, 5, 8, 9, 11 and 12 every 21 days for 8 cycles.

<b>Arm title</b>	Placebo Comparator: Placebo + Dexamethasone + Bortezomib
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Arm description:

Placebo administered once IV on Day 1 every 21 days for 8 cycles.

Dexamethasone 20 mg administered once orally on Days 1, 2, 4, 5, 8, 9, 11 and 12 every 21 days for 8 cycles.

Bortezomib 1.3 mg/m<sup>2</sup> administered once SQ on Days 1, 4, 8 and 11 every 21 days for 8 cycles.

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Placebo administered once IV on Day 1 every 21 days for 8 cycles.

Investigational medicinal product name	Dexamethasone
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Dexamethasone 20 mg administered once orally on Days 1, 2, 4, 5, 8, 9, 11 and 12 every 21 days for 8 cycles.

Investigational medicinal product name	Bortezomib
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Bortezomib 1.3 mg/m<sup>2</sup> administered once SQ on Days 1, 4, 8 and 11 every 21 days for 8 cycles.

Number of subjects in period 1	100 mg Tabalumab+Dexamethasone+Bortezomib	300 mg Tabalumab+Dexamethasone+Bortezomib	Placebo Comparator: Placebo + Dexamethasone + Bortezomib
Started	74	74	72
Received at Least 1 Dose of Study Drug	73	74	72
Completed	66	66	66
Not completed	8	8	6
Consent withdrawn by subject	5	3	3
Adverse event, non-fatal	-	1	-
Investigator Decision	1	-	-
Sponsor Decision	2	3	2
Lost to follow-up	-	-	1
Protocol deviation	-	1	-

## Baseline characteristics

### Reporting groups

Reporting group title	100 mg Tabalumab+Dexamethasone+Bortezomib
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Reporting group description:

Tabalumab 100 milligram (mg) administered once intravenously (IV) over 30 minutes on Day 1 every 21 days for 8 cycles.

Dexamethasone 20 mg administered once orally on Days 1, 2, 4, 5, 8, 9, 11 and 12 every 21 days for 8 cycles.

Bortezomib 1.3 milligram per square meter (mg/m<sup>2</sup>) administered once subcutaneously (SQ) on Days 1, 4, 8 and 11 every 21 days for 8 cycles.

Reporting group title	300 mg Tabalumab+Dexamethasone+Bortezomib
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Reporting group description:

Tabalumab 300 mg administered once IV over 30 minutes on Day 1 every 21 days for 8 cycles.

Dexamethasone 20 mg administered orally on Days 1, 2, 4, 5, 8, 9, 11 and 12 every 21 days for 8 cycles.

Bortezomib 1.3 mg/m<sup>2</sup> administered once SQ on Days 1, 4, 8 and 11 every 21 days for 8 cycles.

Reporting group title	Placebo Comparator: Placebo + Dexamethasone + Bortezomib
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Reporting group description:

Placebo administered once IV on Day 1 every 21 days for 8 cycles.

Dexamethasone 20 mg administered once orally on Days 1, 2, 4, 5, 8, 9, 11 and 12 every 21 days for 8 cycles.

Bortezomib 1.3 mg/m<sup>2</sup> administered once SQ on Days 1, 4, 8 and 11 every 21 days for 8 cycles.

Reporting group values	100 mg Tabalumab+Dexame thasone+Bortezomib	300 mg Tabalumab+Dexame thasone+Bortezomib	Placebo Comparator: Placebo + Dexamethasone + Bortezomib
Number of subjects	74	74	72
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	37	30	32
From 65-84 years	36	43	40
85 years and over	1	1	0
Age Continuous Units: years			
median	63.2	65.7	65.4
standard deviation	± 11.01	± 9.11	± 9.50
Gender categorical Units: Subjects			
Female	44	37	32
Male	30	37	40

Sex: Female, Male			
Units: Subjects			
Female	44	37	32
Male	30	37	40
Ethnicity (NIH/OMB)			
Units: Subjects			
Hispanic or Latino	4	3	5
Not Hispanic or Latino	39	50	35
Unknown or Not Reported	31	21	32
Race (NIH/OMB)			
Units: Subjects			
American Indian or Alaska Native	3	1	2
Asian	14	18	13
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	1	2	2
White	56	53	53
More than one race	0	0	0
Unknown or Not Reported	0	0	2
Region of Enrollment			
Units: Subjects			
United States	11	9	9
United Kingdom	5	7	4
Spain	8	5	8
Greece	6	7	9
Canada	2	2	0
South Korea	6	9	8
Netherlands	0	0	1
Turkey	6	7	4
Taiwan	7	6	5
Brazil	4	2	5
Poland	4	13	7
Italy	7	2	3
Mexico	3	1	2
France	3	3	6
Germany	2	1	1

<b>Reporting group values</b>	Total		
Number of subjects	220		
Age categorical			
Units: Subjects			
In utero	0		
Preterm newborn infants (gestational age < 37 wks)	0		
Newborns (0-27 days)	0		
Infants and toddlers (28 days-23 months)	0		
Children (2-11 years)	0		
Adolescents (12-17 years)	0		
Adults (18-64 years)	99		
From 65-84 years	119		
85 years and over	2		



Age Continuous Units: years median standard deviation	-		
Gender categorical Units: Subjects			
Female	113		
Male	107		
Sex: Female, Male Units: Subjects			
Female	113		
Male	107		
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	12		
Not Hispanic or Latino	124		
Unknown or Not Reported	84		
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	6		
Asian	45		
Native Hawaiian or Other Pacific Islander	0		
Black or African American	5		
White	162		
More than one race	0		
Unknown or Not Reported	2		
Region of Enrollment Units: Subjects			
United States	29		
United Kingdom	16		
Spain	21		
Greece	22		
Canada	4		
South Korea	23		
Netherlands	1		
Turkey	17		
Taiwan	18		
Brazil	11		
Poland	24		
Italy	12		
Mexico	6		
France	12		
Germany	4		

## End points

### End points reporting groups

Reporting group title	100 mg Tabalumab+Dexamethasone+Bortezomib
Reporting group description:	
Tabalumab 100 milligram (mg) administered once intravenously (IV) over 30 minutes on Day 1 every 21 days for 8 cycles.	
Dexamethasone 20 mg administered once orally on Days 1, 2, 4, 5, 8, 9, 11 and 12 every 21 days for 8 cycles.	
Bortezomib 1.3 milligram per square meter (mg/m <sup>2</sup> ) administered once subcutaneously (SQ) on Days 1, 4, 8 and 11 every 21 days for 8 cycles.	
Reporting group title	300 mg Tabalumab+Dexamethasone+Bortezomib
Reporting group description:	
Tabalumab 300 mg administered once IV over 30 minutes on Day 1 every 21 days for 8 cycles.	
Dexamethasone 20 mg administered orally on Days 1, 2, 4, 5, 8, 9, 11 and 12 every 21 days for 8 cycles.	
Bortezomib 1.3 mg/m <sup>2</sup> administered once SQ on Days 1, 4, 8 and 11 every 21 days for 8 cycles.	
Reporting group title	Placebo Comparator: Placebo + Dexamethasone + Bortezomib
Reporting group description:	
Placebo administered once IV on Day 1 every 21 days for 8 cycles.	
Dexamethasone 20 mg administered once orally on Days 1, 2, 4, 5, 8, 9, 11 and 12 every 21 days for 8 cycles.	
Bortezomib 1.3 mg/m <sup>2</sup> administered once SQ on Days 1, 4, 8 and 11 every 21 days for 8 cycles.	

### Primary: Progression Free Survival (PFS)

End point title	Progression Free Survival (PFS)
End point description:	
PFS is defined as the time from date of first dose to the first observation of disease progression or death due to any cause. If a participant does not have a complete baseline disease assessment, then the PFS time is censored at the enrollment date, regardless of whether or not objectively determined disease progression (Increase of > 25% from lowest response in serum M component, urine M component, bone marrow plasma cell percentage, development of bone lesions) or death has been observed for the participant. If a participant is not known to have died or have objective progression as of the data inclusion cutoff date for the analysis, the PFS time is censored at the last complete objective progression-free disease assessment date.	
End point type	Primary
End point timeframe:	
Baseline up to Objective Disease Progression or Death From Any Cause (9 months)	

End point values	100 mg Tabalumab+Dexamethasone+Bortezomib	300 mg Tabalumab+Dexamethasone+Bortezomib	Placebo Comparator: Placebo + Dexamethasone + Bortezomib	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	74 <sup>[1]</sup>	74 <sup>[2]</sup>	72 <sup>[3]</sup>	
Units: months				
median (confidence interval 95%)	6.6 (5.6 to 8.5)	7.5 (5.8 to 9.3)	7.6 (6.5 to 9.3)	

Notes:

[1] - All randomized participants.

[2] - All randomized participants.

[3] - All randomized participants.

## Statistical analyses

<b>Statistical analysis title</b>	Statistical Analysis 1
Comparison groups	300 mg Tabalumab+Dexamethasone+Bortezomib v Placebo Comparator: Placebo + Dexamethasone + Bortezomib v 100 mg Tabalumab+Dexamethasone+Bortezomib
Number of subjects included in analysis	220
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0187
Method	nominal one-sided p-value

## Secondary: Overall Survival

End point title	Overall Survival
End point description: Overall survival is the duration from enrollment to death from any cause. For participants who were alive, overall survival was censored at the last contact. 9999 is the equivalent for N/A as medians were not reached for the timeframe.	
End point type	Secondary
End point timeframe: Baseline to Death From Any Cause (19 months)	

<b>End point values</b>	100 mg Tabalumab+De xamethasone+ Bortezomib	300 mg Tabalumab+De xamethasone+ Bortezomib	Placebo Comparator: Placebo + Dexamethason e + Bortezomib	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	74 <sup>[4]</sup>	74 <sup>[5]</sup>	72 <sup>[6]</sup>	
Units: months				
median (confidence interval 95%)	9999 (9999 to 9999)	9999 (9999 to 9999)	9999 (9999 to 9999)	

Notes:

[4] - Medians were not reached for timeframe, no data to report.

[5] - Medians were not reached for timeframe, no data to report.

[6] - Medians were not reached for timeframe, no data to report.

## Statistical analyses

No statistical analyses for this end point

## Secondary: Time to First Skeletal-Related Event (SRE)

End point title	Time to First Skeletal-Related Event (SRE)
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**End point description:**

Time to first SRE is defined as time from randomization to any one of the following related to multiple myeloma: New Pathological Fracture, Spinal Cord Compression, Surgery to the Bone, Radiation to the Bone collected until participant death, study closure or lost to follow up. Participants not known to have had an SRE at the time of the analysis were censored at the date of their last complete documented assessment for SRE. 9999 is the equivalent for N/A as medians were not reached for the timeframe.

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End point type	Secondary
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**End point timeframe:**

Baseline to Date of First Skeletal Related Event (19 months)

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End point values	100 mg Tabalumab+De xamethasone+ Bortezomib	300 mg Tabalumab+De xamethasone+ Bortezomib	Placebo Comparator: Placebo + Dexamethason e + Bortezomib	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	74 <sup>[7]</sup>	74 <sup>[8]</sup>	72 <sup>[9]</sup>	
Units: months				
median (confidence interval 95%)	9999 (9999 to 9999)	9999 (19.8 to 9999)	9999 (9999 to 9999)	

**Notes:**

[7] - Medians were not reached for timeframe, no data to report.

[8] - Medians were not reached for timeframe, no data to report.

[9] - Medians were not reached for timeframe, no data to report.

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**Statistical analyses**

No statistical analyses for this end point

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**Secondary: Number of Participants with >30% Reduction in Brief Pain Inventory (BPI) - Worst Pain Score**

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End point title	Number of Participants with >30% Reduction in Brief Pain Inventory (BPI) - Worst Pain Score
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**End point description:**

BPI is assessed by 7 questions rated "0" for "no pain" and higher numbers indicated more pain.

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End point type	Secondary
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**End point timeframe:**

Baseline through End of Treatment (19 months)

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End point values	100 mg Tabalumab+De xamethasone+ Bortezomib	300 mg Tabalumab+De xamethasone+ Bortezomib	Placebo Comparator: Placebo + Dexamethason e + Bortezomib	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	74 <sup>[10]</sup>	74 <sup>[11]</sup>	72 <sup>[12]</sup>	
Units: Participants				
number (not applicable)	37	30	30	

Notes:

[10] - All randomized participants.

[11] - All randomized participants.

[12] - All randomized participants.

## Statistical analyses

No statistical analyses for this end point

### Secondary: Time to Progression (TTP)

End point title	Time to Progression (TTP)
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End point description:

Time to progression is defined as the time from the date of randomization to the date of first observed objective progression or death due to study disease. Time to progression will be censored as for PFS for those participants not known to have progressed or that died from other causes.

End point type	Secondary
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End point timeframe:

Baseline to Objective Disease Progression or Death (9 months)

End point values	100 mg Tabalumab+De xamethasone+ Bortezomib	300 mg Tabalumab+De xamethasone+ Bortezomib	Placebo Comparator: Placebo + Dexamethason e + Bortezomib	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	74 <sup>[13]</sup>	74 <sup>[14]</sup>	72 <sup>[15]</sup>	
Units: months				
median (confidence interval 95%)	6.6 (5.9 to 9.3)	8.2 (6.4 to 11.2)	8.1 (6.9 to 9.5)	

Notes:

[13] - All randomized participants.

[14] - All randomized participants.

[15] - All randomized participants.

## Statistical analyses

No statistical analyses for this end point

### Secondary: Duration of Response (DoR)

End point title	Duration of Response (DoR)
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End point description:

DOR is measured from the date of first evidence of a confirmed response to the date of objective progression or the date of death due to any cause, whichever is earlier. If a responder is not known to have died or have objective progression as of the data inclusion cutoff date, the DOR time will be censored at the last complete objective progression-free disease assessment date.

End point type	Secondary
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End point timeframe:

Time from Response to Objective Disease Progression (38 months)

End point values	100 mg Tabalumab+De xamethasone+ Bortezomib	300 mg Tabalumab+De xamethasone+ Bortezomib	Placebo Comparator: Placebo + Dexamethason e + Bortezomib	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	43 <sup>[16]</sup>	44 <sup>[17]</sup>	44 <sup>[18]</sup>	
Units: months				
median (confidence interval 95%)	7.9 (6.0 to 11.6)	8.6 (6.5 to 10.7)	7.7 (5.8 to 13.1)	

Notes:

[16] - All randomized participants who received at least 1 dose of study drug and had a response.

[17] - All randomized participants who received at least 1 dose of study drug and had a response.

[18] - All randomized participants who received at least 1 dose of study drug and had a response.

### Statistical analyses

No statistical analyses for this end point

### Secondary: Time to Next Treatment (TNT)

End point title	Time to Next Treatment (TNT)
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End point description:

TNT is defined as the time from the date of randomization to the date of initiation of the first poststudy treatment course of anticancer therapy or death from any cause. Time to next treatment will be censored at the date of the last visit for participant who did not initiate additional anticancer therapy.

End point type	Secondary
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End point timeframe:

Baseline to Initiation of New Cancer Treatment or Death From Any Cause (18 Months)

End point values	100 mg Tabalumab+De xamethasone+ Bortezomib	300 mg Tabalumab+De xamethasone+ Bortezomib	Placebo Comparator: Placebo + Dexamethason e + Bortezomib	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	74 <sup>[19]</sup>	74 <sup>[20]</sup>	72 <sup>[21]</sup>	
Units: months				
median (confidence interval 95%)	10.1 (7.0 to 11.9)	9.9 (6.8 to 14.8)	11.7 (7.8 to 17.5)	

Notes:

[19] - All randomized participants.

[20] - All randomized participants.

[21] - All randomized participants.

### Statistical analyses

No statistical analyses for this end point

### Secondary: Pharmacokinetics (PK): Maximum Concentration (Cmax) of Tabalumab

End point title	Pharmacokinetics (PK): Maximum Concentration (Cmax) of Tabalumab <sup>[22]</sup>
End point description: Maximum Concentration (Cmax) of Tabalumab. Baseline, Cycle 1: Day 1 pre to LY2127399 dose, post Bortezomib (BTZ) dose, 2 hours post dose (hrs pd), Day 4:pre BTZ dose, Day 8:Pre BTZ dose, Day 11: pre BTZ dose, BTZ pd Cycle 2 Day 1 pre LY2127399 dose, BTZ pd, Day 4: anytime, Day 8 anytime, Day 11 anytime Cycle 3 - completion of study: Day 1 pre LY2127399 dose, BTZ pd with week 6-10 considered Steady State	
End point type	Secondary
End point timeframe: See Outcome Measure description for time frame	

Notes:

[22] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Only arms that received tabalumab were reported.

End point values	100 mg Tabalumab+De xamethasone+ Bortezomib	300 mg Tabalumab+De xamethasone+ Bortezomib		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	68 <sup>[23]</sup>	71 <sup>[24]</sup>		
Units: micrograms per milliliter				
geometric mean (geometric coefficient of variation)				
Cycle 1	38.0 (± 39)	103 (± 43)		
Cycle 2	47.9 (± 51)	131 (± 40)		
Steady State (Cycle 6-10)	69.0 (± 51)	189 (± 54)		

Notes:

[23] - All randomized participants with evaluable PK data.

[24] - All randomized participants with evaluable PK data.

## Statistical analyses

No statistical analyses for this end point

## Secondary: PK: Time to Maximum Plasma Concentration (Tmax) of Tabalumab

End point title	PK: Time to Maximum Plasma Concentration (Tmax) of Tabalumab <sup>[25]</sup>
End point description: Baseline, Cycle 1: Day 1 pre to LY2127399 dose, post BTZ dose, 2 hours post dose (hrs pd), Day 4:pre BTZ dose, Day 8:Pre BTZ dose, Day 11: pre BTZ dose, BTZ pd Cycle 2 Day 1 pre LY2127399 dose, BTZ pd, Day 4: anytime, Day 8 anytime, Day 11 anytime Cycle 3 - completion of study: Day 1 pre LY2127399 dose, BTZ pd with week 6-10 considered Steady State	
End point type	Secondary
End point timeframe: See Outcome Measure description for time frame	

Notes:

[25] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Only arms that received tabalumab were reported.

End point values	100 mg Tabalumab+De xamethasone+ Bortezomib	300 mg Tabalumab+De xamethasone+ Bortezomib		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	73 <sup>[26]</sup>	74 <sup>[27]</sup>		
Units: hours				
arithmetic mean (confidence interval 95%)				
Cycle 1	1.5 (0.75 to 503.75)	1.58 (0.92 to 162.58)		
Cycle 2	0.92 (0.47 to 503.77)	0.76 (0.5 to 503.58)		
Steady State (Cycle 6-10)	0.75 (0.338 to 9.92)	0.73 (0 to 1.75)		

Notes:

[26] - All randomized participants with evaluable PK data.

[27] - All randomized participants with evaluable PK data.

## Statistical analyses

No statistical analyses for this end point

## Secondary: PK: Area Under the Curve Over the Dosing Interval (AUC-T) for Tabalumab

End point title	PK: Area Under the Curve Over the Dosing Interval (AUC-T) for Tabalumab <sup>[28]</sup>
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End point description:

Baseline, Cycle 1: Day 1 pre to LY2127399 dose, post BTZ dose, 2 hours post dose (hrs pd), Day 4: pre BTZ dose, Day 8: Pre BTZ dose, Day 11: pre BTZ dose, BTZ pd  
Cycle 2 Day 1 pre LY2127399 dose, BTZ pd, Day 4: anytime, Day 8 anytime, Day 11 anytime  
Cycle 3 - completion of study: Day 1 pre LY2127399 dose, BTZ pd with week 6-10 considered Steady State

End point type	Secondary
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End point timeframe:

See Outcome Measure description for time frame

Notes:

[28] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Only arms that received tabalumab were reported.

End point values	100 mg Tabalumab+De xamethasone+ Bortezomib	300 mg Tabalumab+De xamethasone+ Bortezomib		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	68 <sup>[29]</sup>	63 <sup>[30]</sup>		
Units: micrograms times hour per milliliter				
geometric mean (geometric coefficient of variation)				
Cycle 1	7790 (± 42)	2220 (± 44)		
Cycle 2	11600 (± 36)	35400 (± 49)		
Steady State (Cycle 6-10)	25300 (± 57)	70100 (± 52)		



Notes:

[29] - All randomized participants with evaluable PK data.

[30] - All randomized participants with evaluable PK data.

## Statistical analyses

No statistical analyses for this end point

### Secondary: Number of Participants Developing Anti-tabalumab Antibodies

End point title	Number of Participants Developing Anti-tabalumab Antibodies
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End point description:

End point type	Secondary
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End point timeframe:

Baseline through Cycle 8

End point values	100 mg Tabalumab+De xamethasone+ Bortezomib	300 mg Tabalumab+De xamethasone+ Bortezomib	Placebo Comparator: Placebo + Dexamethason e + Bortezomib	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	0 <sup>[31]</sup>	0 <sup>[32]</sup>	0 <sup>[33]</sup>	
Units: Participants				
number (not applicable)				

Notes:

[31] - Zero participants analyzed due to insufficient sample collection.

[32] - Zero participants analyzed due to insufficient sample collection.

[33] - Zero participants analyzed due to insufficient sample collection.

## Statistical analyses

No statistical analyses for this end point

### Secondary: Participants with Best Overall Response (BOR) in Each Category

End point title	Participants with Best Overall Response (BOR) in Each Category
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End point description:

Stringent Complete Response-Complete Response and normal free light chain ration and no clonal cells in bone marrow Complete Response- no monoclonal protein (mp) in blood, no serum or urine mp, less than 5% plasma cells in bone marrow Very Good Partial Response-more than 90% decrease in mp and urine protein Partial Response- over 50% decrease in serum mp Stable Disease- less than 25 percent decrease of monoclonal protein Progressive Disease- 25% increase compared to lowest value of serum mp, urine mp, no measurable mp

End point type	Secondary
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End point timeframe:

Baseline to Objective Disease Progression or Initiation of New Cancer Treatment (28 Months)

<b>End point values</b>	100 mg Tabalumab+De xamethasone+ Bortezomib	300 mg Tabalumab+De xamethasone+ Bortezomib	Placebo Comparator: Placebo + Dexamethason e + Bortezomib	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	74 <sup>[34]</sup>	74 <sup>[35]</sup>	72 <sup>[36]</sup>	
Units: participants				
number (not applicable)				
Stringent Complete Response	1	0	2	
Complete Response	10	4	4	
Very Good Partial Response	10	16	9	
Partial Response	23	23	29	
Minimal Response	6	8	6	
Stable Disease	14	10	12	
Progressive Disease	6	7	6	

Notes:

[34] - All randomized participants.

[35] - All randomized participants.

[36] - All randomized participants.

## Statistical analyses

No statistical analyses for this end point

## Secondary: Number of Participants with a Given Best Objective Myeloma Response (Quality of Response [QoR])

End point title	Number of Participants with a Given Best Objective Myeloma Response (Quality of Response [QoR]) <sup>[37]</sup>
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End point description:

Quality of response was classified into ordered categories of sCR, CR, VGPR, PR, MR, SD, or PD, according to the International Uniform Response Criteria for Multiple Myeloma, that is, sCR > CR > VGPR > PR > MR > SD > PD. The quality of response was evaluated as an ordinal outcome using a logistic regression model. Independent variables in the analysis include treatment, baseline stratification factors of ISS risk category (high risk, low risk), number of lines of prior therapy (1, >1), baseline disease assessment method (SPEP/UPEP, SFLC), response to prior bortezomib therapy (bortezomib naïve or ≥PR lasting 6 months or longer, MR or PR lasting less than 6 months), and C - 1 threshold effects, where C is the number of response categories analyzed.

End point type	Secondary
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End point timeframe:

Baseline to Objective Disease Progression or Initiation of New Cancer Treatment ( 28 Months)

Notes:

[37] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: The logistic regression model comparing the 2 tabalumab arms is able to identify a trend for improved response in 1 cohort over another.

End point values	100 mg Tabalumab+De xamethasone+ Bortezomib	300 mg Tabalumab+De xamethasone+ Bortezomib		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	74 <sup>[38]</sup>	74 <sup>[39]</sup>		
Units: odds ratio				
number (not applicable)	1.84	1.98		

Notes:

[38] - All randomized participants.

[39] - All randomized participants.

## Statistical analyses

No statistical analyses for this end point

## Secondary: Overall Response Rate (ORR)

End point title	Overall Response Rate (ORR)
End point description: Overall Response Rate (ORR) is the proportion of participants that had a response.	
End point type	Secondary
End point timeframe: Baseline to Objective Disease Progression or Initiation of New Cancer Treatment (28 Months)	

End point values	100 mg Tabalumab+De xamethasone+ Bortezomib	300 mg Tabalumab+De xamethasone+ Bortezomib	Placebo Comparator: Placebo + Dexamethason e + Bortezomib	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	74 <sup>[40]</sup>	74 <sup>[41]</sup>	72 <sup>[42]</sup>	
Units: percentage of participants				
number (not applicable)	58.1	59.5	61.1	

Notes:

[40] - All randomized participants who had a partial response or greater.

[41] - All randomized participants who had a partial response or greater.

[42] - All randomized participants who had a partial response or greater.

## Statistical analyses

No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

Entire Study

Adverse event reporting additional description:

H9S-MC-JDCG

Assessment type	Systematic
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### Dictionary used

Dictionary name	MedDRA
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Dictionary version	17.0
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### Reporting groups

Reporting group title	Placebo Comparator: Placebo + Dexamethasone + Bortezomib
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Reporting group description:

Placebo administered once IV on Day 1 every 21 days for 8 cycles.

Dexamethasone 20 mg administered once orally on Days 1, 2, 4, 5, 8, 9, 11 and 12 every 21 days for 8 cycles.

Bortezomib 1.3 mg/m<sup>2</sup> administered once SQ on Days 1, 4, 8 and 11 every 21 days for 8 cycles.

Reporting group title	300 mg Tabalumab+Dexame thasone+Bortezomib
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Reporting group description:

Tabalumab 300 mg administered once IV over 30 minutes on Day 1 every 21 days for 8 cycles.

Dexamethasone 20 mg administered orally on Days 1, 2, 4, 5, 8, 9, 11 and 12 every 21 days for 8 cycles.

Bortezomib 1.3 mg/m<sup>2</sup> administered once SQ on Days 1, 4, 8 and 11 every 21 days for 8 cycles.

Reporting group title	100 mg Tabalumab+Dexame thasone+Bortezomib
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Reporting group description:

Tabalumab 100 milligram (mg) administered once intravenously (IV) over 30 minutes on Day 1 every 21 days for 8 cycles.

Dexamethasone 20 mg administered once orally on Days 1, 2, 4, 5, 8, 9, 11 and 12 every 21 days for 8 cycles.

Bortezomib 1.3 milligram per square meter (mg/m<sup>2</sup>) administered once subcutaneously (SQ) on Days 1, 4, 8 and 11 every 21 days for 8 cycles.

Serious adverse events	Placebo Comparator: Placebo + Dexamethasone + Bortezomib	300 mg Tabalumab+Dexame thasone+Bortezomib	100 mg Tabalumab+Dexame thasone+Bortezomib
Total subjects affected by serious adverse events			
subjects affected / exposed	26 / 72 (36.11%)	35 / 74 (47.30%)	33 / 73 (45.21%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
acute myeloid leukaemia			
alternative dictionary used: MedDRA 17.0			

subjects affected / exposed	0 / 72 (0.00%)	1 / 74 (1.35%)	0 / 73 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
colorectal cancer			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	0 / 72 (0.00%)	1 / 74 (1.35%)	0 / 73 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
hepatic neoplasm			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	0 / 72 (0.00%)	0 / 74 (0.00%)	1 / 73 (1.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
plasma cell leukaemia			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	0 / 72 (0.00%)	0 / 74 (0.00%)	1 / 73 (1.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
plasma cell myeloma			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	1 / 72 (1.39%)	2 / 74 (2.70%)	0 / 73 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
deep vein thrombosis			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	1 / 72 (1.39%)	0 / 74 (0.00%)	1 / 73 (1.37%)
occurrences causally related to treatment / all	1 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
haemorrhage			
alternative dictionary used: MedDRA 17.0			

subjects affected / exposed	0 / 72 (0.00%)	0 / 74 (0.00%)	1 / 73 (1.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
hypotension alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	0 / 72 (0.00%)	1 / 74 (1.35%)	0 / 73 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
hypovolaemic shock alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	0 / 72 (0.00%)	0 / 74 (0.00%)	1 / 73 (1.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
orthostatic hypotension alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	1 / 72 (1.39%)	0 / 74 (0.00%)	1 / 73 (1.37%)
occurrences causally related to treatment / all	1 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
shock haemorrhagic alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	0 / 72 (0.00%)	1 / 74 (1.35%)	0 / 73 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
asthenia alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	1 / 72 (1.39%)	0 / 74 (0.00%)	0 / 73 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
disease progression alternative dictionary used: MedDRA 17.0			

subjects affected / exposed	0 / 72 (0.00%)	0 / 74 (0.00%)	1 / 73 (1.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
fatigue			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	1 / 72 (1.39%)	0 / 74 (0.00%)	0 / 73 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
general physical health deterioration			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	1 / 72 (1.39%)	1 / 74 (1.35%)	2 / 73 (2.74%)
occurrences causally related to treatment / all	0 / 1	0 / 1	1 / 3
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 1
localised oedema			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	1 / 72 (1.39%)	0 / 74 (0.00%)	0 / 73 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
multi-organ failure			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	1 / 72 (1.39%)	1 / 74 (1.35%)	2 / 73 (2.74%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 1	0 / 1	0 / 2
oedema peripheral			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	1 / 72 (1.39%)	0 / 74 (0.00%)	0 / 73 (0.00%)
occurrences causally related to treatment / all	3 / 3	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
pyrexia			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	2 / 72 (2.78%)	2 / 74 (2.70%)	1 / 73 (1.37%)
occurrences causally related to treatment / all	0 / 2	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Respiratory, thoracic and mediastinal disorders			
acute respiratory failure			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	0 / 72 (0.00%)	0 / 74 (0.00%)	1 / 73 (1.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
chronic obstructive pulmonary disease			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	1 / 72 (1.39%)	1 / 74 (1.35%)	0 / 73 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
dyspnoea			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	0 / 72 (0.00%)	0 / 74 (0.00%)	1 / 73 (1.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
interstitial lung disease			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	1 / 72 (1.39%)	0 / 74 (0.00%)	0 / 73 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
pleural effusion			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	0 / 72 (0.00%)	0 / 74 (0.00%)	1 / 73 (1.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
pneumonitis			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	1 / 72 (1.39%)	1 / 74 (1.35%)	0 / 73 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Investigations			



platelet count decreased alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	1 / 72 (1.39%)	1 / 74 (1.35%)	1 / 73 (1.37%)
occurrences causally related to treatment / all	1 / 1	1 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
renal function test abnormal alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	1 / 72 (1.39%)	0 / 74 (0.00%)	0 / 73 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
troponin increased alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	1 / 72 (1.39%)	0 / 74 (0.00%)	0 / 73 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
fall alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	1 / 72 (1.39%)	1 / 74 (1.35%)	1 / 73 (1.37%)
occurrences causally related to treatment / all	0 / 1	1 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
femur fracture alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	1 / 72 (1.39%)	1 / 74 (1.35%)	0 / 73 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
humerus fracture alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	0 / 72 (0.00%)	1 / 74 (1.35%)	0 / 73 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
injury alternative dictionary used: MedDRA 17.0			

subjects affected / exposed	0 / 72 (0.00%)	0 / 74 (0.00%)	1 / 73 (1.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
multiple fractures			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	0 / 72 (0.00%)	0 / 74 (0.00%)	1 / 73 (1.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
subdural haemorrhage			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	0 / 72 (0.00%)	0 / 74 (0.00%)	1 / 73 (1.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
thoracic vertebral fracture			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	0 / 72 (0.00%)	0 / 74 (0.00%)	1 / 73 (1.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
traumatic haemorrhage			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	0 / 72 (0.00%)	0 / 74 (0.00%)	1 / 73 (1.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Congenital, familial and genetic disorders			
left ventricle outflow tract obstruction			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	0 / 72 (0.00%)	0 / 74 (0.00%)	1 / 73 (1.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
acute coronary syndrome			
alternative dictionary used: MedDRA 17.0			

subjects affected / exposed	0 / 72 (0.00%)	1 / 74 (1.35%)	0 / 73 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
acute myocardial infarction			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	0 / 72 (0.00%)	1 / 74 (1.35%)	0 / 73 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
angina pectoris			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	0 / 72 (0.00%)	1 / 74 (1.35%)	0 / 73 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
atrial fibrillation			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	0 / 72 (0.00%)	1 / 74 (1.35%)	0 / 73 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
cardiac arrest			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	0 / 72 (0.00%)	1 / 74 (1.35%)	0 / 73 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 6	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
cardiac failure			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	0 / 72 (0.00%)	1 / 74 (1.35%)	1 / 73 (1.37%)
occurrences causally related to treatment / all	0 / 0	0 / 2	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ventricular dysfunction			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	0 / 72 (0.00%)	0 / 74 (0.00%)	1 / 73 (1.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1

Nervous system disorders			
altered state of consciousness			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	0 / 72 (0.00%)	1 / 74 (1.35%)	0 / 73 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
autonomic neuropathy			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	0 / 72 (0.00%)	0 / 74 (0.00%)	1 / 73 (1.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ischaemic stroke			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	0 / 72 (0.00%)	0 / 74 (0.00%)	1 / 73 (1.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
loss of consciousness			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	0 / 72 (0.00%)	0 / 74 (0.00%)	2 / 73 (2.74%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
neuropathy peripheral			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	1 / 72 (1.39%)	0 / 74 (0.00%)	0 / 73 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
peripheral sensory neuropathy			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	2 / 72 (2.78%)	1 / 74 (1.35%)	0 / 73 (0.00%)
occurrences causally related to treatment / all	3 / 3	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
anaemia			
alternative dictionary used: MedDRA 17.0			

subjects affected / exposed	2 / 72 (2.78%)	2 / 74 (2.70%)	2 / 73 (2.74%)
occurrences causally related to treatment / all	0 / 2	0 / 2	0 / 3
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
febrile neutropenia			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	0 / 72 (0.00%)	0 / 74 (0.00%)	3 / 73 (4.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
leukopenia			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	1 / 72 (1.39%)	0 / 74 (0.00%)	0 / 73 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
neutropenia			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	0 / 72 (0.00%)	1 / 74 (1.35%)	0 / 73 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
thrombocytopenia			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	1 / 72 (1.39%)	1 / 74 (1.35%)	3 / 73 (4.11%)
occurrences causally related to treatment / all	0 / 1	0 / 1	1 / 3
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Gastrointestinal disorders			
colitis			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	0 / 72 (0.00%)	0 / 74 (0.00%)	1 / 73 (1.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
constipation			
alternative dictionary used: MedDRA 17.0			

subjects affected / exposed	1 / 72 (1.39%)	1 / 74 (1.35%)	1 / 73 (1.37%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
diarrhoea			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	1 / 72 (1.39%)	2 / 74 (2.70%)	3 / 73 (4.11%)
occurrences causally related to treatment / all	1 / 1	2 / 2	3 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
gastric perforation			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	0 / 72 (0.00%)	0 / 74 (0.00%)	1 / 73 (1.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ileus paralytic			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	0 / 72 (0.00%)	1 / 74 (1.35%)	0 / 73 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
intestinal ischaemia			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	1 / 72 (1.39%)	0 / 74 (0.00%)	0 / 73 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	1 / 1	0 / 0	0 / 0
large intestinal haemorrhage			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	0 / 72 (0.00%)	0 / 74 (0.00%)	1 / 73 (1.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
melaena			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	1 / 72 (1.39%)	0 / 74 (0.00%)	0 / 73 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

nausea alternative dictionary used: MedDRA 17.0 subjects affected / exposed	1 / 72 (1.39%)	0 / 74 (0.00%)	0 / 73 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
upper gastrointestinal haemorrhage alternative dictionary used: MedDRA 17.0 subjects affected / exposed	0 / 72 (0.00%)	1 / 74 (1.35%)	0 / 73 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
vomiting alternative dictionary used: MedDRA 17.0 subjects affected / exposed	0 / 72 (0.00%)	1 / 74 (1.35%)	0 / 73 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders cholecystitis alternative dictionary used: MedDRA 17.0 subjects affected / exposed	0 / 72 (0.00%)	1 / 74 (1.35%)	0 / 73 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
cholecystitis acute alternative dictionary used: MedDRA 17.0 subjects affected / exposed	0 / 72 (0.00%)	0 / 74 (0.00%)	1 / 73 (1.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Renal and urinary disorders haematuria alternative dictionary used: MedDRA 17.0 subjects affected / exposed	1 / 72 (1.39%)	0 / 74 (0.00%)	0 / 73 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
incontinence alternative dictionary used: MedDRA 17.0			

subjects affected / exposed	1 / 72 (1.39%)	0 / 74 (0.00%)	0 / 73 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
renal failure			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	2 / 72 (2.78%)	0 / 74 (0.00%)	1 / 73 (1.37%)
occurrences causally related to treatment / all	0 / 2	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
renal failure acute			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	5 / 72 (6.94%)	4 / 74 (5.41%)	3 / 73 (4.11%)
occurrences causally related to treatment / all	1 / 5	0 / 4	1 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
back pain			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	1 / 72 (1.39%)	1 / 74 (1.35%)	0 / 73 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
bone pain			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	0 / 72 (0.00%)	1 / 74 (1.35%)	0 / 73 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
muscular weakness			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	0 / 72 (0.00%)	1 / 74 (1.35%)	0 / 73 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
musculoskeletal pain			
alternative dictionary used: MedDRA 17.0			



subjects affected / exposed	1 / 72 (1.39%)	0 / 74 (0.00%)	0 / 73 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
pathological fracture			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	1 / 72 (1.39%)	0 / 74 (0.00%)	0 / 73 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
bacteraemia			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	0 / 72 (0.00%)	0 / 74 (0.00%)	2 / 73 (2.74%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
brain abscess			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	0 / 72 (0.00%)	0 / 74 (0.00%)	1 / 73 (1.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
bronchopneumonia			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	0 / 72 (0.00%)	0 / 74 (0.00%)	2 / 73 (2.74%)
occurrences causally related to treatment / all	0 / 0	0 / 0	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
cellulitis			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	0 / 72 (0.00%)	0 / 74 (0.00%)	1 / 73 (1.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
cytomegalovirus colitis			
alternative dictionary used: MedDRA 17.0			

subjects affected / exposed	0 / 72 (0.00%)	0 / 74 (0.00%)	1 / 73 (1.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
diverticulitis			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	1 / 72 (1.39%)	1 / 74 (1.35%)	0 / 73 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
helicobacter infection			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	0 / 72 (0.00%)	0 / 74 (0.00%)	1 / 73 (1.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
herpes zoster			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	1 / 72 (1.39%)	2 / 74 (2.70%)	1 / 73 (1.37%)
occurrences causally related to treatment / all	0 / 1	1 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
infection			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	0 / 72 (0.00%)	2 / 74 (2.70%)	0 / 73 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
infectious colitis			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	0 / 72 (0.00%)	1 / 74 (1.35%)	0 / 73 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
influenza			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	0 / 72 (0.00%)	0 / 74 (0.00%)	1 / 73 (1.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

lobar pneumonia alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	1 / 72 (1.39%)	1 / 74 (1.35%)	1 / 73 (1.37%)
occurrences causally related to treatment / all	1 / 1	1 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
lower respiratory tract infection alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	0 / 72 (0.00%)	1 / 74 (1.35%)	1 / 73 (1.37%)
occurrences causally related to treatment / all	0 / 0	2 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
otitis media alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	0 / 72 (0.00%)	0 / 74 (0.00%)	1 / 73 (1.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
pneumococcal sepsis alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	0 / 72 (0.00%)	0 / 74 (0.00%)	1 / 73 (1.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
pneumocystis jiroveci pneumonia alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	0 / 72 (0.00%)	0 / 74 (0.00%)	1 / 73 (1.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
pneumonia alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	5 / 72 (6.94%)	3 / 74 (4.05%)	9 / 73 (12.33%)
occurrences causally related to treatment / all	1 / 5	0 / 3	7 / 11
deaths causally related to treatment / all	0 / 1	0 / 1	0 / 1
pneumonia haemophilus alternative dictionary used: MedDRA 17.0			

subjects affected / exposed	0 / 72 (0.00%)	1 / 74 (1.35%)	0 / 73 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
respiratory syncytial virus infection alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	0 / 72 (0.00%)	0 / 74 (0.00%)	1 / 73 (1.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
respiratory tract infection alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	0 / 72 (0.00%)	2 / 74 (2.70%)	0 / 73 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
sepsis alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	0 / 72 (0.00%)	5 / 74 (6.76%)	2 / 73 (2.74%)
occurrences causally related to treatment / all	0 / 0	1 / 5	0 / 3
deaths causally related to treatment / all	0 / 0	1 / 4	0 / 1
septic shock alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	0 / 72 (0.00%)	0 / 74 (0.00%)	4 / 73 (5.48%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 8
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 3
sinusitis alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	0 / 72 (0.00%)	0 / 74 (0.00%)	1 / 73 (1.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
soft tissue infection alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	0 / 72 (0.00%)	2 / 74 (2.70%)	0 / 73 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

upper respiratory tract infection alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	1 / 72 (1.39%)	2 / 74 (2.70%)	0 / 73 (0.00%)
occurrences causally related to treatment / all	0 / 1	1 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
urinary tract infection alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	1 / 72 (1.39%)	0 / 74 (0.00%)	2 / 73 (2.74%)
occurrences causally related to treatment / all	0 / 1	0 / 0	2 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
wound infection alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	0 / 72 (0.00%)	1 / 74 (1.35%)	0 / 73 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
decreased appetite alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	0 / 72 (0.00%)	2 / 74 (2.70%)	0 / 73 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
dehydration alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	1 / 72 (1.39%)	1 / 74 (1.35%)	0 / 73 (0.00%)
occurrences causally related to treatment / all	1 / 1	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
diabetes mellitus alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	0 / 72 (0.00%)	0 / 74 (0.00%)	1 / 73 (1.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
hyperglycaemia alternative dictionary used: MedDRA 17.0			

subjects affected / exposed	0 / 72 (0.00%)	0 / 74 (0.00%)	1 / 73 (1.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
hypovolaemia			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	0 / 72 (0.00%)	0 / 74 (0.00%)	1 / 73 (1.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Frequency threshold for reporting non-serious adverse events: 5 %

<b>Non-serious adverse events</b>	Placebo Comparator: Placebo + Dexamethasone + Bortezomib	300 mg Tabalumab+Dexame thasone+Bortezomib	100 mg Tabalumab+Dexame thasone+Bortezomib
Total subjects affected by non-serious adverse events			
subjects affected / exposed	69 / 72 (95.83%)	72 / 74 (97.30%)	71 / 73 (97.26%)
Vascular disorders			
orthostatic hypotension			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	5 / 72 (6.94%)	4 / 74 (5.41%)	3 / 73 (4.11%)
occurrences (all)	6	5	4
General disorders and administration site conditions			
asthenia			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	9 / 72 (12.50%)	6 / 74 (8.11%)	7 / 73 (9.59%)
occurrences (all)	9	6	11
face oedema			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	2 / 72 (2.78%)	4 / 74 (5.41%)	1 / 73 (1.37%)
occurrences (all)	2	4	2
fatigue			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	26 / 72 (36.11%)	27 / 74 (36.49%)	28 / 73 (38.36%)
occurrences (all)	47	49	38
injection site erythema			

alternative dictionary used: MedDRA 17.0 subjects affected / exposed occurrences (all)	1 / 72 (1.39%) 1	2 / 74 (2.70%) 5	4 / 73 (5.48%) 4
injection site reaction alternative dictionary used: MedDRA 17.0 subjects affected / exposed occurrences (all)	3 / 72 (4.17%) 7	3 / 74 (4.05%) 5	6 / 73 (8.22%) 13
oedema alternative dictionary used: MedDRA 17.0 subjects affected / exposed occurrences (all)	4 / 72 (5.56%) 25	4 / 74 (5.41%) 35	1 / 73 (1.37%) 5
oedema peripheral alternative dictionary used: MedDRA 17.0 subjects affected / exposed occurrences (all)	8 / 72 (11.11%) 27	15 / 74 (20.27%) 69	14 / 73 (19.18%) 57
pain alternative dictionary used: MedDRA 17.0 subjects affected / exposed occurrences (all)	2 / 72 (2.78%) 3	3 / 74 (4.05%) 3	6 / 73 (8.22%) 7
pyrexia alternative dictionary used: MedDRA 17.0 subjects affected / exposed occurrences (all)	6 / 72 (8.33%) 8	10 / 74 (13.51%) 13	11 / 73 (15.07%) 13
Reproductive system and breast disorders benign prostatic hyperplasia alternative dictionary used: MedDRA 17.0 subjects affected / exposed <sup>[1]</sup> occurrences (all)	1 / 40 (2.50%) 1	0 / 37 (0.00%) 0	2 / 29 (6.90%) 2
Respiratory, thoracic and mediastinal disorders cough alternative dictionary used: MedDRA 17.0 subjects affected / exposed occurrences (all)	13 / 72 (18.06%) 18	16 / 74 (21.62%) 17	8 / 73 (10.96%) 9
dyspnoea			

alternative dictionary used: MedDRA 17.0 subjects affected / exposed occurrences (all)  epistaxis alternative dictionary used: MedDRA 17.0 subjects affected / exposed occurrences (all)	11 / 72 (15.28%)  16   1 / 72 (1.39%)  1	8 / 74 (10.81%)  8   3 / 74 (4.05%)  3	9 / 73 (12.33%)  10   4 / 73 (5.48%)  8
Psychiatric disorders depression alternative dictionary used: MedDRA 17.0 subjects affected / exposed occurrences (all)  insomnia alternative dictionary used: MedDRA 17.0 subjects affected / exposed occurrences (all)	4 / 72 (5.56%)  4   11 / 72 (15.28%)  24	5 / 74 (6.76%)  5   15 / 74 (20.27%)  19	1 / 73 (1.37%)  1   12 / 73 (16.44%)  12
Investigations alanine aminotransferase increased alternative dictionary used: MedDRA 17.0 subjects affected / exposed occurrences (all)  aspartate aminotransferase increased alternative dictionary used: MedDRA 17.0 subjects affected / exposed occurrences (all)  blood alkaline phosphatase increased alternative dictionary used: MedDRA 17.0 subjects affected / exposed occurrences (all)  blood cholesterol increased alternative dictionary used: MedDRA 17.0 subjects affected / exposed occurrences (all)  lymphocyte count decreased alternative dictionary used:	1 / 72 (1.39%)  2   1 / 72 (1.39%)  1   0 / 72 (0.00%)  0   6 / 72 (8.33%)  10	6 / 74 (8.11%)  6   6 / 74 (8.11%)  6   4 / 74 (5.41%)  5   2 / 74 (2.70%)  6	8 / 73 (10.96%)  11   7 / 73 (9.59%)  9   3 / 73 (4.11%)  5   5 / 73 (6.85%)  12



MedDRA 17.0			
subjects affected / exposed	1 / 72 (1.39%)	5 / 74 (6.76%)	1 / 73 (1.37%)
occurrences (all)	1	13	1
neutrophil count decreased			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	1 / 72 (1.39%)	2 / 74 (2.70%)	4 / 73 (5.48%)
occurrences (all)	5	3	8
platelet count decreased			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	8 / 72 (11.11%)	7 / 74 (9.46%)	16 / 73 (21.92%)
occurrences (all)	15	10	46
weight decreased			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	5 / 72 (6.94%)	8 / 74 (10.81%)	5 / 73 (6.85%)
occurrences (all)	5	11	7
weight increased			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	3 / 72 (4.17%)	3 / 74 (4.05%)	4 / 73 (5.48%)
occurrences (all)	5	3	4
Injury, poisoning and procedural complications			
contusion			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	2 / 72 (2.78%)	5 / 74 (6.76%)	3 / 73 (4.11%)
occurrences (all)	3	5	3
Cardiac disorders			
atrial fibrillation			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	3 / 72 (4.17%)	2 / 74 (2.70%)	4 / 73 (5.48%)
occurrences (all)	3	2	4
Nervous system disorders			
dizziness			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	16 / 72 (22.22%)	15 / 74 (20.27%)	6 / 73 (8.22%)
occurrences (all)	23	20	7
dysgeusia			

alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	2 / 72 (2.78%)	3 / 74 (4.05%)	5 / 73 (6.85%)
occurrences (all)	2	4	5
headache			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	5 / 72 (6.94%)	3 / 74 (4.05%)	9 / 73 (12.33%)
occurrences (all)	9	4	10
hypoaesthesia			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	1 / 72 (1.39%)	0 / 74 (0.00%)	4 / 73 (5.48%)
occurrences (all)	1	0	5
neuralgia			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	7 / 72 (9.72%)	9 / 74 (12.16%)	1 / 73 (1.37%)
occurrences (all)	10	12	1
neuropathy peripheral			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	13 / 72 (18.06%)	11 / 74 (14.86%)	17 / 73 (23.29%)
occurrences (all)	25	16	20
paraesthesia			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	5 / 72 (6.94%)	8 / 74 (10.81%)	8 / 73 (10.96%)
occurrences (all)	6	11	12
peripheral sensory neuropathy			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	17 / 72 (23.61%)	19 / 74 (25.68%)	10 / 73 (13.70%)
occurrences (all)	31	32	16
tremor			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	1 / 72 (1.39%)	0 / 74 (0.00%)	4 / 73 (5.48%)
occurrences (all)	1	0	4
Blood and lymphatic system disorders			
anaemia			
alternative dictionary used: MedDRA 17.0			

subjects affected / exposed	17 / 72 (23.61%)	13 / 74 (17.57%)	25 / 73 (34.25%)
occurrences (all)	24	25	52
neutropenia			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	6 / 72 (8.33%)	4 / 74 (5.41%)	6 / 73 (8.22%)
occurrences (all)	6	11	8
thrombocytopenia			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	23 / 72 (31.94%)	8 / 74 (10.81%)	16 / 73 (21.92%)
occurrences (all)	60	26	34
Eye disorders			
vision blurred			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	4 / 72 (5.56%)	1 / 74 (1.35%)	2 / 73 (2.74%)
occurrences (all)	4	1	2
Gastrointestinal disorders			
abdominal distension			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	5 / 72 (6.94%)	5 / 74 (6.76%)	8 / 73 (10.96%)
occurrences (all)	8	5	13
abdominal pain			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	5 / 72 (6.94%)	6 / 74 (8.11%)	5 / 73 (6.85%)
occurrences (all)	6	6	8
abdominal pain upper			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	3 / 72 (4.17%)	4 / 74 (5.41%)	5 / 73 (6.85%)
occurrences (all)	4	4	5
constipation			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	23 / 72 (31.94%)	26 / 74 (35.14%)	19 / 73 (26.03%)
occurrences (all)	30	32	31
diarrhoea			
alternative dictionary used: MedDRA 17.0			

subjects affected / exposed	21 / 72 (29.17%)	27 / 74 (36.49%)	28 / 73 (38.36%)
occurrences (all)	27	40	44
dyspepsia			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	8 / 72 (11.11%)	7 / 74 (9.46%)	5 / 73 (6.85%)
occurrences (all)	10	9	5
nausea			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	14 / 72 (19.44%)	11 / 74 (14.86%)	15 / 73 (20.55%)
occurrences (all)	18	12	19
stomatitis			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	3 / 72 (4.17%)	5 / 74 (6.76%)	1 / 73 (1.37%)
occurrences (all)	3	5	2
toothache			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	1 / 72 (1.39%)	0 / 74 (0.00%)	4 / 73 (5.48%)
occurrences (all)	1	0	4
vomiting			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	9 / 72 (12.50%)	5 / 74 (6.76%)	6 / 73 (8.22%)
occurrences (all)	9	8	7
Skin and subcutaneous tissue disorders			
erythema			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	0 / 72 (0.00%)	5 / 74 (6.76%)	1 / 73 (1.37%)
occurrences (all)	0	8	1
pruritus			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	0 / 72 (0.00%)	5 / 74 (6.76%)	1 / 73 (1.37%)
occurrences (all)	0	6	1
rash			
alternative dictionary used: MedDRA 17.0			

subjects affected / exposed	2 / 72 (2.78%)	7 / 74 (9.46%)	7 / 73 (9.59%)
occurrences (all)	6	16	16
Musculoskeletal and connective tissue disorders			
arthralgia			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	3 / 72 (4.17%)	7 / 74 (9.46%)	5 / 73 (6.85%)
occurrences (all)	4	7	5
back pain			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	13 / 72 (18.06%)	12 / 74 (16.22%)	7 / 73 (9.59%)
occurrences (all)	16	14	10
muscular weakness			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	6 / 72 (8.33%)	4 / 74 (5.41%)	6 / 73 (8.22%)
occurrences (all)	9	5	7
musculoskeletal chest pain			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	4 / 72 (5.56%)	0 / 74 (0.00%)	7 / 73 (9.59%)
occurrences (all)	4	0	8
musculoskeletal pain			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	4 / 72 (5.56%)	4 / 74 (5.41%)	4 / 73 (5.48%)
occurrences (all)	5	5	4
myalgia			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	5 / 72 (6.94%)	3 / 74 (4.05%)	6 / 73 (8.22%)
occurrences (all)	7	3	7
pain in extremity			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	11 / 72 (15.28%)	10 / 74 (13.51%)	6 / 73 (8.22%)
occurrences (all)	11	14	11
Infections and infestations			
herpes zoster			
alternative dictionary used: MedDRA 17.0			

subjects affected / exposed	4 / 72 (5.56%)	6 / 74 (8.11%)	4 / 73 (5.48%)
occurrences (all)	5	7	4
nasopharyngitis			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	2 / 72 (2.78%)	4 / 74 (5.41%)	3 / 73 (4.11%)
occurrences (all)	2	4	5
pneumonia			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	3 / 72 (4.17%)	3 / 74 (4.05%)	6 / 73 (8.22%)
occurrences (all)	3	4	7
respiratory tract infection			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	0 / 72 (0.00%)	3 / 74 (4.05%)	8 / 73 (10.96%)
occurrences (all)	0	4	14
sinusitis			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	0 / 72 (0.00%)	4 / 74 (5.41%)	3 / 73 (4.11%)
occurrences (all)	0	4	3
upper respiratory tract infection			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	20 / 72 (27.78%)	18 / 74 (24.32%)	11 / 73 (15.07%)
occurrences (all)	27	31	17
urinary tract infection			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	5 / 72 (6.94%)	4 / 74 (5.41%)	8 / 73 (10.96%)
occurrences (all)	5	4	12
Metabolism and nutrition disorders			
decreased appetite			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	8 / 72 (11.11%)	12 / 74 (16.22%)	12 / 73 (16.44%)
occurrences (all)	10	13	13
dehydration			
alternative dictionary used: MedDRA 17.0			

subjects affected / exposed	5 / 72 (6.94%)	1 / 74 (1.35%)	3 / 73 (4.11%)
occurrences (all)	7	1	5
hyperglycaemia			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	7 / 72 (9.72%)	5 / 74 (6.76%)	5 / 73 (6.85%)
occurrences (all)	11	10	11
hyperkalaemia			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	5 / 72 (6.94%)	1 / 74 (1.35%)	3 / 73 (4.11%)
occurrences (all)	7	1	3
hypocalcaemia			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	1 / 72 (1.39%)	7 / 74 (9.46%)	7 / 73 (9.59%)
occurrences (all)	1	9	12
hypokalaemia			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	3 / 72 (4.17%)	7 / 74 (9.46%)	7 / 73 (9.59%)
occurrences (all)	3	8	12
hyponatraemia			
alternative dictionary used: MedDRA 17.0			
subjects affected / exposed	3 / 72 (4.17%)	4 / 74 (5.41%)	3 / 73 (4.11%)
occurrences (all)	4	4	3

Notes:

[1] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.

Justification: This event is gender specific, only occurring in male subjects. The number of subjects exposed has been adjusted accordingly.

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

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### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported